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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/581,773	02/12/2007	Hans J. Stauss	28646/42100	7037

4743 7590 07/13/2010

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EXAMINER	
SKELDING, ZACHARY S	
ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
07/13/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,773	STAUSS ET AL.	
	Examiner	Art Unit	
	ZACHARY SKELDING	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-22,25 and 28-32* is/are pending in the application.

4a) Of the above claim(s) *20-22,25,31 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-19 and 28-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments and remarks filed May 4, 2010 are acknowledged.

   Claims 12-19, 20-22, 25 and 28-32 are pending.

   Claims 12-19 and 28-30 are under consideration.

   Claims 20-22, 25, 31 and 32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on October 1, 2009.

2. The previous rejection of record can be found in the Office Action mailed January 4, 2010.

   The previous rejections under 35 U.S.C. § 101 have been withdrawn in view of applicant's amendments to the claims.

   The previous objections to the claims have been withdrawn in view of applicant's amendments to the claims.

   New Grounds of Rejection necessitated by applicant's amendments to the claims are put forth below.

3. The specification stands objected to because it contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s): as stated in the Office Action mailed January 4, 2010 at page 2, Section 2, the "Schedule of SEQ ID NOs." on page 17 is not sufficient to fully identify these sequences as required by the rules. Rather, each occurrence of a polynucleotide or polypeptide sequence as defined by the rules must be accompanied by the identifier "SEQ ID NO: __". Appropriate correction is still required.

4. 35 U.S.C. §101 states:

   Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 17-19 and 28-30 are rejected under 35 USC §101 because the claimed invention is directed to non-statutory subject matter.

   This is a New Grounds of Rejection necessitated by applicant's amendments to the claims.

The instant claims reciting "a host cell comprising a polynucleotide…" do not sufficiently distinguish over the product that exists naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. Note that this rejection is being applied to claims reciting "a host cell…which is a T cell derived from a patient" because this phrase does not necessarily refer to an isolated host cell, it could merely further describe the host cell. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or "purified" in the preamble. See MPEP 2105.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 12-19 and 28-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This is a New Grounds of Rejection necessitated by applicant's amendments to the claims.

On the one hand claims 12-14 could be interpreted as claims where the language "or encoding a modified TCR alpha chain portion / or encoding a modified TCR beta chain portion / or encoding a modified single chain TCR molecule" is shorthand for something like "or wherein said TCR alpha chain portion is a modified TCR alpha chain portion / or wherein said TCR beta chain portion is a modified TCR beta chain portion / or wherein said single chain TCR is a modified single chain TCR molecule," i.e., what is being claimed is something limited to taking the unique sequences recited in the first part of each of these claims and then making modification to these unique sequences.

On the other hand claims 12-14 could be interpreted as claims where the language "or encoding a modified TCR alpha chain portion / or encoding a modified TCR beta chain portion / or encoding a modified single chain TCR molecule" is to be interpreted literally, as in the "modified...portion/molecule" refers to *any* TCR that has been selected for its ability to bind a HLA-A2/RMFPNAPYL complex and then modified according to the claims.

Yet another interpretation is that the claims encompass in their breadth all of the above.

These interpretations are different in that each gives the claims ever greater breadth, with the first interpretation being more limited than the second.

Thus, the instant claims fail to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 12-16 stand rejected, and newly amended or added claims 17-19 and 28-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

an isolated polynucleotide encoding a T cell receptor (TCR) alpha chain portion containing three CDRs: CDR1α: SSYSPS (SEQ ID NO: 2), CDR2α: YTSAATL, and CDR3α: SPFSGGGADGLT (SEQ ID NO: 5), wherein a TCR containing the alpha chain portion encoded by said polynucleotide and a TCR beta chain portion containing three CDRs: CDR1β: DFQATT (SEQ ID NO: 6), CDR2β: SNEGSKA (SEQ ID NO: 7), and CDR3β: RDGGEGSETQY (SEQ ID NO: 9) binds an HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex, and

an isolated polynucleotide encoding a T cell receptor (TCR) beta chain portion containing three CDRs: CDR1β: DFQATT (SEQ ID NO: 6), CDR2β: SNEGSKA (SEQ ID NO: 7), and CDR3β: RDGGEGSETQY (SEQ ID NO: 9), wherein a TCR containing the beta chain portion encoded by said polynucleotide and a TCR alpha chain portion containing three CDRs: CDR1α: SSYSPS (SEQ ID NO: 2), CDR2α: YTSAATL, and CDR3α: SPFSGGGADGLT (SEQ ID NO: 5) binds an HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex, and

an isolated polynucleotide encoding a single chain TCR molecule containing an alpha chain portion and a beta chain portion wherein the alpha chain portion contains three CDRs: CDR1α: SSYSPS (SEQ ID NO: 2), CDR2α: YTSAATL, and CDR3α: SPFSGGGADGLT (SEQ ID NO: 5), and wherein the beta chain portion contains three CDRs: CDR1β: DFQATT (SEQ ID NO: 6), CDR2β: SNEGSKA (SEQ ID NO: 7), and CDR3β: RDGGEGSETQY (SEQ ID NO: 9), wherein the TCR encoded by said polynucleotide binds an HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex,

does not reasonably provide enablement for the claimed invention which encompasses in its breadth nucleic acids encoding TCRs based on the particular CDR sequences recited in claims 12-14 having up to three residues in one or more CDR replaced by another amino acid residue, essentially for the reasons of record as put forth in the Office Action mailed January 4, 2010 as described further below.

Applicant argues the claims are enabled for the following reasons:

"…the skilled person could readily identify CDR sequences with up to three variations having the desired properties without undue experimentation. Such sequence modifications are well known in the art and have been carried out for a number of different polypeptides. A person of skill in the art can take a wild-type TCR molecule and introduce random mutations into the CDRs using a mutagenesis experiment (e.g. phage display or yeast display), and select for the sequences which retain their TCR recognition specificity and have a greater affinity for the target antigen of interest (HLA- A2/RMFPNAPYL complex as recited in claims 12-14) than the wild-type molecule. In other words, the framework sequence remains intact, but a few amino acid sequence modifications have been introduced to enhance TCR affinity.

As evidence that this would not be an undue burden, Applicants enclose the document Li et al., Nature Biotechnology, 23(3):349 (2005) (Exhibit A), which discloses the directed evolution of high-affinity TCRs specific for two different peptide-human leukocyte antigen complexes. Clearly, using the methods described by Li et al, the skilled person would be able to mutagenise the TCR sequences listed in the claims, and arrive at a TCR molecule with greater affinity for HLA-A2/RFMPNAPYL complex without undue experimentation."

Applicant's argument has been considered but has not been found convincing essentially for the reasons of record as put forth in the Office Action mailed January 4, 2010 as described further below.

Li teaches the following at page 349 left col., 1st paragraph – col. bridging paragraph:

"Phage display of a single-chain mouse TCR has also been reported, but high-affinity TCR generation was not achieved. ***These technologies have therefore not had the impact of monoclonal-antibody library display, and there remains a need for a robust technology that allows display and molecular evolution of TCRs.*** Recently we have described a method for producing stable TCR molecules that involves introducing an interchain disulfide bond into the interface between the TCR constant domains and which is applicable to a wide range of different TCRs. Such disulfide-stabilized TCRs can be expressed in a number of different systems (N. Pumphrey et al., unpublished data) and retain the authentic structure of a heterodimeric αβ-TCR. The versatility of this approach and the unique stability of disulfide-linked TCRs ***led us to explore the possibility of displaying them on the surface of bacteriophage.***"

Li concludes their paper with the following:

"…[t]he TCR phage display technology we have described here provides a generic approach for the affinity maturation of TCRs, as has been possible for antibodies for many years. Antibody phage display has also been used for the study of antibody-antigen interactions, structure-function relations and antibody folding and stability, and for the generation of novel human antibodies from naive libraries, thereby bypassing the immune system and its

selection mechanisms. We expect that ***this technology will now enable all of these to be achieved in the future*** for the study and selection of TCRs.

(emphasis added to both).

From the quotes above it appears Li is teaching their disclosure of a method for directed evolution of TCR using phage display to be new to the art. However, Li was published after applicant's effective filing date.

This is important because the state of the art existing at the filing date of the application is used to determine whether a particular disclosure is enabling as of the filing date. >Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1325-26 (Fed. Cir. 2004) ("a patent document cannot enable technology that arises after the date of application").< Publications dated after the filing date providing information publicly first disclosed after the filing date generally cannot be used to show what was known at the time of filing. In re Gunn, 537 F.2d 1123, 1128, 190 USPQ 402,405-06 (CCPA 1976); In re Budnick, 537 F.2d 535, 538, 190 USPQ 422, 424 (CCPA 1976) (In general, if an applicant seeks to use a patent to prove the state of the art for the purpose of the enablement requirement, the patent must have an issue date earlier than the effective filing date of the application.). While a later dated publication cannot supplement an insufficient disclosure in a prior dated application to make it enabling, applicant can offer the testimony of an expert based on the publication as evidence of the level of skill in the art at the time the application was filed. Gould v. Quigg, 822 F.2d 1074, 1077, 3 USPQ2d 1302, 1304 (Fed. Cir. 1987). See MPEP 2164.05(a).

Thus, because Li was not state of the art as of applicant's filing date it is unclear how "using the methods described by Li et al, the skilled person would be able to mutagenise the TCR sequences listed in the claims, and arrive at a TCR molecule with greater affinity for HLA-A2/RFMPNAPYL complex" as argued by applicant.

Moreover, even if Li were published prior to applicant's effective priority date, the skilled artisan would still not be enabled to make the breadth of the TCRs encompassed in the instant claims in the absence of undue experimentation.

For example, Li teaches at page 349, right col., 1st paragraph that "High affinity TCRs selected from A6 TCR–phage libraries contained mutations only in the CDR3β chains (Table 2a), but this was almost certainly due to minor technical problems with the A6 CDR3α libraries, which were resolved for generation of the 1G4 TCR–phage library, resulting in the selection of many high-affinity variants containing CDR3α mutations from these libraries (Table 2b)."

However, Li does not make clear what "minor technical problems with the A6 CDR3α libraries" gave rise to this bias for CDR3β only mutations in the A6 library or what was changed to give the result observed with the 1G4 TCR-phage library. Thus, the skilled artisan would have substantial doubt about their ability to successfully practice this method.

Moreover, Li did not attempt to mutagenize CDR1. Given that TCR CDRs 1 and 2 are responsible for binding to the MHC as would be well known to the skilled artisan, see, e.g., Janeway, Immunobiology, 2001, Garland Publishing at page 262-63 bridging paragraph, the skilled artisan would further be quite uncertain if it is possible to mutagenize all three TCR CDRs from both chains simultaneously and obtain a TCR having greater affinity for an HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex compared to the non-mutagenized TCR. More specifically, would such a mutagenesis and selection strategy give the desired result or be akin to changing too many variables simultaneously such that the mutagenized TCR will always have a lower affinity for the HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex?

Thus, the skilled artisan would not be able to make the claimed invention to its full breadth without first making a substantial inventive contribution to the method described by Li.

The instant claims encompass an invention of tremendous breadth, and essentially call for trial and error by the skilled artisan to begin discovering how to make and use the claimed invention without assisting the skilled artisan in such an endeavor, which is insufficient to constitute adequate enablement.

As put forth in Rasmusson v. SmithKline Beecham Corp., 75 USPQ2d 1297-1303 (CAFC 2005), "[i]f mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to 'inventions' consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the 'inventor' would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis."

Similarly, a patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of Genentech, Inc, v. Novo Nordisk, 42 USPQ 2d 1001,(CAFC 1997), the court held: "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". Further, "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one cannot follow the guidance presented therein to make the claimed TCR without first making a substantial inventive contribution.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 12-14 stand rejected and newly amended or added claims 15-19 and 28-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, essentially for the reasons of record as put forth in the Office Action mailed January 4, 2010 as described further below.

Applicant argues they have amended the claims as suggested by the Examiner to specify the peptide RMFPNAPYL bound to an HLA-A2 molecule.

Applicant's argument has been considered but has not been found convincing essentially for the reasons of record as put forth in the Office Action mailed January 4, 2010 as described further below.

The examiner did not suggest applicant amend the claims as currently presented.

The issue with the claims is that they still encompass in their breadth polynucleotides encoding TCR alpha and/or beta chains with particular CDRs but the claims do not recite which antigen is bound by the encoded polypeptide chain(s) (see claims 12-14 reading from the preamble of each up to the phrase "or encoding..."). Other than binding to the peptide RMFPNAPYL bound to an HLA-A2 class I molecule the instant specification gives no guidance or direction as to other cancer antigens that can be bound by the claimed TCR. Thus, the instant specification does not establish possession of the genus of polynucleotides encoding "alpha/beta chain portion" or "single chain TCR" recited in the instant claims that bind to the genus of cancer antigens.

Applicant has not described the claimed invention sufficiently to show they had possession of the claimed genus of polynucleotides encoding "alpha/beta chain portion" or "single chain TCR" recited in the instant claims that bind to the genus of cancer antigens.

Furthermore, the claims as they currently stand also encompass in their breadth, for example, nucleic acids encoding TCRs based on the particular CDR sequences recited in claims 12-14 having up to three residues in one or more CDR replaced by another amino acid residue where said TCR has a greater affinity for an HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex than an unmodified TCR.

While applicant is in possession of an isolated polynucleotide encoding a T cell receptor (TCR) alpha chain portion containing three CDRs: CDR1α: SSYSPS (SEQ ID NO: 2), CDR2α: YTSAATL, and CDR3α: SPFSGGGADGLT (SEQ ID NO: 5), wherein a TCR containing the alpha chain portion encoded by said polynucleotide and a TCR beta chain portion containing three CDRs: CDR1β: DFQATT (SEQ ID NO: 6), CDR2β: SNEGSKA

(SEQ ID NO: 7), and CDR3β: RDGGEGSETQY (SEQ ID NO: 9) binds an HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex, and

an isolated polynucleotide encoding a T cell receptor (TCR) beta chain portion containing three CDRs: CDR1β: DFQATT (SEQ ID NO: 6), CDR2β: SNEGSKA (SEQ ID NO: 7), and CDR3β: RDGGEGSETQY (SEQ ID NO: 9), wherein a TCR containing the beta chain portion encoded by said polynucleotide and a TCR alpha chain portion containing three CDRs: CDR1α: SSYSPS (SEQ ID NO: 2), CDR2α: YTSAATL, and CDR3α: SPFSGGGADGLT (SEQ ID NO: 5) binds an HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex, and

an isolated polynucleotide encoding a single chain TCR molecule containing an alpha chain portion and a beta chain portion wherein the alpha chain portion contains three CDRs: CDR1α: SSYSPS (SEQ ID NO: 2), CDR2α: YTSAATL, and CDR3α: SPFSGGGADGLT (SEQ ID NO: 5), and wherein the beta chain portion contains three CDRs: CDR1β: DFQATT (SEQ ID NO: 6), CDR2β: SNEGSKA (SEQ ID NO: 7), and CDR3β: RDGGEGSETQY (SEQ ID NO: 9), wherein the TCR encoded by said polynucleotide binds an HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex,

Applicant is not in possession of the claimed invention which encompasses in its breadth nucleic acids encoding TCRs based on the particular CDR sequences recited in claims 12-14 having up to three residues in one or more CDR replaced by another amino acid residue.

The instant specification discloses a single TCR which specifically binds the peptide RMFPNAPYL bound to an HLA-A2 class I molecule. (see pages 18-19). The instant specification further discloses how to make CDR variants in general, but provides no specific guidance about how to make variants of the single disclosed TCR (see, e.g., page 7, 1st paragraph).

Neither the instant specification nor the knowledge in the art provide sufficient direction or guidance to put applicant in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the extensive variation permitted within the claimed genus of polynucleotides encoding TCR alpha and/or beta chains.

The instant specification does not provide adequate written description of the broad genus of polynucleotides encoding TCR alpha and/or beta chains encompassed by instant claims because relevant identifying characteristics for the polynucleotides encoding TCR alpha and/or beta chains encompassed by this claim, such as the particular *structural or other physical and/or chemical characteristics that are critical to the function* of the claimed polynucleotide encoding TCRs, i.e., having a greater affinity for an HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex than an unmodified TCR, are not disclosed.

The instant specification does not provide sufficient direction or guidance to establish possession of the breadth of the claimed genus for the reasons stated in Section 9 above with

respect to the unpredictability in the art concerning making polynucleotide encoding TCRs encompassed by the breadth of the instant claims.

Without this guidance or direction the skilled artisan would not consider applicant to be in possession of the claimed genus of polynucleotides encoding TCRs because the skilled artisan recognizes that even seemingly minor changes made without guidance or direction as to the relationship between the particular amino acid sequence of the TCR encoded by the claimed polynucleotides and its ability to bind an HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex with greater affinity than unmodified TCR can dramatically affect TCR-complex binding in adverse ways.

Thus, applicant has not described the claimed invention sufficiently to show they had possession of the claimed genus of polynucleotides encoding TCRs. Moreover, neither the instant specification nor the knowledge in the art provide sufficient direction or guidance for the skilled artisan to make the genus of polynucleotides encoding TCRs.

Without a correlation between structure and function, the claim does little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *See Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 ("definition by function … does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is").

Sufficient description to show possession of such a genus "may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1567, 43 USPQ2d 1398, 1405 (Fed. Cir. 1997). Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. *See University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 69 USPQ2d 1886 (Fed. Cir. 2004).

Moreover, according to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, especially page 1106 3rd column, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See, MPEP 2163 II.A.3a.ii. Applicant is directed to the Revised Guidelines for the Examination of Patent Applications Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No.4, pages 1099-1111, Friday January 5, 2001).

12. No claims are allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ZACHARY SKELDING whose telephone number is (571)272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachary Skelding/

Primary Examiner, Art Unit 1644